REMARKS

Claims 17-20 have been canceled in light of the restriction requirement. Claim 21 has been amended to note that "essentially all" of the disulfide bonds in the 2S albumin have been reduced and alkylated. Support for this limitation is found on page 6 of the application beginning at line 28. Claims 23 and 24 add the further limitations of claims 19 and 20 as noted to be permissible by the Examiner. Support for new claim 25 which requires essentially no response in the form of IgE antibody formation is supported in the results shown in Figures 3 and 4 herein as described on page 21 of the specification at lines 1-24.

New claims 26-30 are completely similar to claims 21-25 except that they clarify that the subject is desensitized to an allergic reaction to the same but unmodified 2S albumin which is subsequently administered to the modified form. Support for this clarification (which may be the manner in which the claims were interpreted in the first place) is found, for example, on page 3 of the specification, beginning at line 25 — page 4, line 5.

No new matter is presented and entry of the amendment is respectfully requested.

There is only one outstanding basis for rejection — all claims were rejected as obvious over WO02/074250 (Panacea) in combination with Bartolomé, *et al., Allergol et Immunopathol.* (1997) 25:135-144 (Bartolomé). It is the position of the Office that Panacea teaches that allergens may be reduced and alkylated to disrupt one or more sulfide bonds and that Bartolomé teaches that the 2S albumin allergens of Brazil nut are sulfur-rich allergens, and thus subject to such treatment. (The Examiner also asserts that Panacea teaches that such modified allergens induce production of T-helper-1 mediated subclasses of IgG citing page 3, line 24-page 4, line 30 and page 40, lines 1-29. Applicants are unable to find such a teaching).

While the Examiner is correct that Panacea teaches reduction of disulfide bonds and subsequent alkylation as means to modify allergens, there is no teaching that essentially all of the disulfide bonds be reduced and alkylated so as to result, as required by new claims 25 and 30, that production of IgE in response to the allergen will be completely eliminated.

Bartolomé is cited, apparently, for its focus on Brazil nut 2S albumin of claims 22 and 27 since only peanut albumin is illustrated in Panacea. Not only does Panacea fail to focus on Brazil nut albumin, it also fails to suggest that essentially all of the disulfide bonds be reduced and alkylated. In fact, it appears to teach away from this by stating merely that "one or more" such bonds should be reduced (see Abstract and page 3, lines 24-26). This is insufficient to suggest that essentially all of the disulfide bonds be reduced, even if that could be considered included within the genus that the Office asserts is suggested by Panacea. This was made clear by the decision in *Genetics Institute, LLC, v. Novartis Vaccines & Diagnostics, Inc.*, (Fed. Cir. 2011) 2011 U.S. App. LEXIS 17513, decided August 23, 2011, where claims which required the presence of a specific region of a truncated recombinant Factor VIII were considered non-obvious over claims that included that possibility but did not require it. (The reason claims were compared was that the case involved a potential interference between two issued patents.) Clearly Panacea does not require that essentially all disulfide bonds be reduced, nor does it suggest that it would be desirable to do so.

The desirability of reducing essentially all of these disulfide bonds is verified by the data in the present application as compared to the results (albeit related to mutant peanut allergen) shown in Panacea. Figures 3 and 4 of the present application and the corresponding description on page 21 show that the method of the invention results in the complete elimination of an IgE response. That

is not the case with the modified peanut allergen of Panacea as shown in Figure 57. In many patients, an IgE response was significant.

This is extremely important since the consequences of an IgE response are often catastrophic. Bartolomé demonstrates this on page 137 at the left-hand column where symptoms of an allergic response resulted in confinement to intensive care for 24 hours. With the magnitude of such a response, it is clear that the IgE response should be completely eliminated.

Further, since neither Panacea nor Bartolomé describe conversion of an immune response from a T helper 2-mediated reaction toward a T helper 1-mediated reaction as does the present specification on page 4 lines 1-5, and as needed to desensitize the subject to subsequent administration of the allergen, claims 26-30 are not obvious for this reason as well.

Withdrawal of the rejection is therefore believed proper.

Conclusion

The claims as amended require that essentially all disulfide bonds be reduced and alkylated in order to provide significant desensitization both to the allergen as administered and to subsequent administration of unaltered allergen. There is no suggestion in Panacea that essentially all disulfide bonds be reduced and alkylated; indeed the emphasis in Panacea is on mutating the IgE epitopes. Bartolomé adds nothing to Panacea except to show that Brazil nut 2S albumin is indeed an allergen that depends at least to some extent on conformation for effectiveness. Although the Office asserts that there was no comparison of the noted remaining ability of the reduced subunits to bind IgE to that of the native albumin, it is clear from the binding of the subunits that Bartolomé fails to teach or suggest that altering the conformation *per se* fails to effectively destroy the ability of the allergen to

elicit an IgE response and indeed to desensitize the subject to future administration of the unmodified allergen so as to eliminate completely an IgE response.

For these reasons, the rejection may be withdrawn and claims 21-30 passed to issue.

Should minor matters remain that could be settled over the phone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 677132000200.

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Respectfully submitted,

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